

## Factors associated with gastro-duodenal disease in patients undergoing upper GI endoscopy at the Korle-Bu Teaching Hospital, Accra, Ghana.

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### Abstract

**Background:** There is a high prevalence of gastro-duodenal disease in sub-Saharan Africa. Peptic ulcer disease in dyspeptic patients, 24.5%, was comparable to prevalence of gastro-duodenal disease among symptomatic individuals in developed countries (12 – 25%). Limited data exists regarding its associated risk factors despite accumulating evidence indicating that gastro-duodenal disease is common in Ghana.

**Objectives:** This study investigates risk factors associated with gastro-duodenal disease at the Korle-Bu Teaching Hospital, Accra, Ghana.

**Methods:** This study utilized a cross-sectional design to consecutively recruit patients referred with upper gastro-intestinal symptoms for endoscopy. The study questionnaire was administered to study participants. *Helicobacter pylori* infection was confirmed by rapid-urease examination at endoscopy.

**Results:** Of 242 patients sampled; 64 had duodenal ulcer, 66 gastric ulcer, 27 gastric cancer and 64 non-ulcer dyspepsia. Nineteen (19) had duodenal and gastric ulcer while 2 had gastric ulcer and cancer. A third (32.6%) of patients had history of NSAID-use. *H. pylori* was associated with gastric ulcer ( $p=0.033$ ) and duodenal ulcer ( $p=0.001$ ). There was an increased prevalence of duodenal ulcer in *H. pylori*-infected patients taking NSAIDs,  $P=0.003$ .

**Conclusion:** *H. pylori* was a major risk factor for peptic ulcer disease. However, NSAID-related gastro-duodenal injury has been shown to be common in *H. pylori* infected patients. It highlights the need for awareness of the adverse gastro-intestinal effects in a *H. pylori* endemic area.

**Keywords:** Peptic ulcer, *Helicobacter*, NSAIDs, endoscopy, Ghana.

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### Introduction

Gastro-duodenal disease is common in Africa<sup>1</sup>. Comparative studies showed considerable variation in the prevalence

of duodenal ulceration in different parts of Africa: the coastal region of West Africa and Congo were high prevalence areas while the Northern savannah of Africa was a low prevalence region<sup>2</sup>. The advent of flexible endoscopy in its evaluation increased the sensitivity and specificity of gastro-duodenal disease diagnosis. It has now become apparent that clearly there is a high prevalence of gastro-duodenal disease existing throughout Africa including historically lower prevalence areas<sup>2</sup>. In fact the overall prevalence of peptic ulcer in dyspeptic patients was 24.5% which is represented in the upper range of 12 – 25% of the prevalence of gastro-duodenal disease among symptomatic individuals in developed countries<sup>1</sup>.

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A study at the Korle-Bu Teaching Hospital (KBTH) Endoscopy Unit, the major tertiary centre in Ghana, reviewed 6977 upper gastro-intestinal (GI) endoscopies between January 1995 and December 2002<sup>3</sup>. Chronic duodenal ulcer (DU) 19.6%, gastritis 12.7%, duodenitis 10.2% and oesophagitis 7.5% were the most frequent diagnoses<sup>3</sup>. Normal endoscopic findings were more common in young patients and represented 41.1% of cases<sup>3</sup>. Another study at the KBTH looked at the incidence of *Helicobacter pylori* (*H. pylori*) infection by rapid-urease-testing in 130 Ghanaian patients referred for upper-GI endoscopy<sup>4</sup>. Three-quarters tested positive for *H. pylori*<sup>4</sup>. While 23.5% of *H. pylori*-positive patients had active peptic ulcers, 18.8% of *H. pylori*-negative patients also had ulcer<sup>4</sup>. Out of 43 patients with normal upper-GI endoscopy, 74.4% were *H. pylori*-positive<sup>4</sup>. This emphasizes a complex inter-play of a number of factors (environmental, host, microbial) in the pathogenesis of gastro-duodenal disease in Ghana. Non-steroidal anti-inflammatory drug (NSAID)-use is another of such risk factors for peptic ulcer formation through several mechanisms including suppression of gastric prostaglandin synthesis and interference with the repair of superficial injury<sup>5</sup>. Limited data exists regarding its use and inter-relationship with other important factors such as *H. pylori* in addition to smoking and alcohol consumption, despite accumulating evidence indicating that gastro-duodenal disease is common in Ghana. The objective of this hospital-based study was to investigate the relationship between these risk factors and gastro-duodenal disease in Ghana.

## Methodology

### Study design

This study used a cross-sectional design to consecutively recruit medical in-patients and clinic out-patients referred to the Endoscopy Unit of the KBTH with upper gastro-intestinal symptoms for endoscopy.

### Study setting

Korle-Bu Teaching Hospital has 2,500 beds and is the main tertiary referral centre in Accra serving the majority of the Southern half of Ghana. It offers a breadth of medical and surgical sub-specialty services including gastroenterology and endoscopy. Study participant recruitment and data collection was performed at the Endoscopy Unit, KBTH, between 2010 and 2012. The Endoscopy Unit is staffed by medical and surgical gas-

troenterologists with the support of trained nurses and auxiliary staff. It uses both Olympus and Storz video-endoscopy equipment for endoscopic procedures. It runs eight (three hour) endoscopy sessions per week and offers both upper and lower GI endoscopy services. Each session performs approximately 10 upper endoscopies and 3 lower endoscopies. Procedures performed are both diagnostic and interventional. The latter include injection sclerotherapy, variceal banding, polypectomy, stent insertion and endotherapy for bleeding ulcers.

### Study participants

Medical inpatients and clinic out-patients with gastro-intestinal symptoms referred to the Endoscopy Unit, KBTH were enrolled into the study. Study participants were consecutively recruited at two scheduled endoscopy sessions each week by convenience sampling. All patients were taken explanatory statements of the project and consented prior to endoscopy. Patients with previous *H. pylori* eradication treatment or proton-pump inhibitor-use two weeks preceding endoscopic analysis and patients with oesophageal disease were excluded from further study. Korle-Bu receives out-patient referrals from several primary and specialist centres across Southern Ghana. One hundred and seven (44.2%) were clinic out-patients while 135 (55.8%) were in-patients.

### Study variables, data sources and measurement

Gastro-intestinal symptoms, medications such as NSAID use, alcohol intake and smoking history was taken. Reported gastrointestinal symptoms included dyspepsia as well as vomiting, anorexia, upper GI bleeding, weight loss and dysphagia. Dyspepsia was defined as one or more of the following symptoms: post-prandial fullness, early satiation (inability to eat a normal sized meal) and epigastric pain/burning according to the Rome III criteria<sup>6</sup>.

Upper gastro-intestinal endoscopy was performed using the Olympus CV-160 videoscope. Study participants were given the option of sedation with (intravenous midazolam 2mg) or lignocaine throat spray. *H. pylori* infection was determined by the rapid-urease-*campylobacter*-like-organism (CLO) test on antral biopsies at upper-GI endoscopy (specificity 98%, sensitivity >93%; Cambridge Life Sciences Ltd, Cambridge, UK). Diagnoses captured with the study questionnaire included duodenal ulcer/erosion (DU), gastric ulcer/erosion (GU), gastric carci-

noma (GCA) and non-ulcer dyspepsia. The latter included patients with either endoscopic gastritis only (n=36) or normal endoscopy (n=28). The location and number of lesions were recorded. The diameter of ulcers was measured using the opened biopsy forceps as previously described<sup>7</sup>.

### Statistical methods

Data was first entered into Excel spread-sheet and further analysed by SPSS 16 Program. Chi-square was used to demonstrate differences between observed variables with a p value of <0.05 used to indicate statistical significance. Categorical data was expressed as proportions and presented in tables and bar charts. Ethical approval was granted by the Protocol Review Committee of the University of Ghana Medical School, College of Health Sciences, University of Ghana.

### Results

#### Baseline characteristics of study participants

Approximately eighty patients attended the Endoscopy

Unit, KBTH for upper GI endoscopy each week. Twenty patients were examined each week for eligibility of whom 242 patients were sampled during the study period. Main reasons for non-participation in the study included recent antibiotic or proton-pump inhibitor use. One hundred and fifteen (47.5%) were females and 127 (52.5%) males. The mean age of patients was 51.4 years, SD 18.6, (median 52 yrs; range 15-95 yrs). Sixty-eight-percent (68%) of patients had dyspepsia, the commonest clinical presentation encountered, table 1. Other symptoms included vomiting (6%), haematemesis and/or melaena (14%), anorexia (3%), weight loss (1%). The commonest physical sign was pallor, (25%) n = 61, followed by abdominal tenderness, (14%) n = 34. Twenty-six-percent, (n = 63) did not have any abnormal physical signs, table 1. In this study, presenting clinical features (symptoms, physical signs) were not associated with the endoscopic diagnoses and no combination of symptoms or signs reliably predicted diagnosis.

**Table 1: Symptoms and physical signs elicited in patients enrolled at the Endoscopy Unit, KBTH**

Symptom	N	%
Dyspepsia	165	68.0
Vomiting	6	6.0
Haematemesis and/or melaena	34	14.0
Anorexia	7	3.0
Weight loss	2	1.0
Dysphagia	1	1.0
Other	17	7.0
Total	242	100.0
<b>Physical signs</b>		
Abdominal mass	15	6.2
Abdominal tenderness	34	14.0
Jaundice	5	2.0
Pallor	61	25.2
Obesity	21	8.7
Cachexia	35	14.5
Clubbing	4	1.7
Ascites, hepatomegaly	2	0.8
hepatomegaly	2	0.8
No signs	63	26.0
Total	242	100.0

### Endoscopy and histopathology findings

Following endoscopy, 64 had DU, 66 GU, 27 GCA and 64 non-ulcer dyspepsia (NUD). Additionally, nineteen (19) had both DU and GU while 2 had GU and GCA. Majority (90.8%) of GUs were distal with pre-pyloric ulcers accounting for 55.2% of all GUs (Table 2). A third (34.5%) of patients with GU had multiple (2 or more)

lesions. Most duodenal ulcers were solitary (78.3%), however 19.3% were large (>2cm) and 1 in 5 patients (21.7%) had two or more ulcers. Most cancers were large, involving the gastric antrum and/or body, with 17.2% showing evidence of gastric outlet obstruction (Table 2). Histology on nineteen (19) of the 29 GCA patients confirmed adenocarcinoma in all cases (100%). Fifteen were intestinal while 4 had diffuse-adenocarcinoma.

**Table 2: Endoscopic Characteristics of Gastro-duodenal disease**

	<b>Gastric ulcer (n=87)</b>	<b>Duodenal ulcer (n=83)</b>	<b>Gastric cancer (n=29)</b>
<b>Location</b>			
-Pre-pyloric region	48 (55.2%)		
-Antral	31 (35.6%)		9 (31.0%)
-Body	5 (5.7%)		6 (20.7%)
-Fundal	1 (1.1%)		
-Cardia	1 (1.1%)		5 (17.2%)
-Antral, body & fundal	1 (1.1%)		9 (31.0%)
<b>Total</b>	<b>87</b>		<b>29</b>
<b>Number</b>			
1	57 (65.5%)	65 (78.3%)	
2	10 (11.5%)	5 (6.0%)	
>2 / multiple	20 (23.0%)	13 (15.7%)	
<b>Total</b>	<b>87</b>	<b>83</b>	
<b>Size</b>			
Small < 1cm	13 (14.9%)	6 (7.2%)	0
1-2cm	64 (73.6%)	61 (73.5%)	4 (13.8%)
Large >2cm	10 (11.5%)	16 (19.3%)	25 (86.2%)
<b>Total</b>	<b>87</b>	<b>83</b>	<b>29</b>
<b>Haemorrhage</b>			
Active bleeding	6 (6.9%)	10 (12.0%)	1 (3.4%)
Clean ulcer base	81 (93.1%)	73 (88.0%)	28 (96.6%)
<b>Total</b>	<b>87</b>	<b>83</b>	<b>29</b>

### Factors associated with gastro-duodenal disease

There was a strong association between GU prevalence and age with 63.1% over 50 years ( $p = 0.0001$ ); GUs were also more common in males (60.9% vs. 39.1 %;  $p = 0.049$ ). Conversely, DUs did not demonstrate a significant relationship with either age or gender. Eighty-percent (80%) of patients with GCA were over 50 years.

Table 3 illustrates the prevalence of *H. pylori* in patients

with non-ulcer dyspepsia, gastric ulcer, duodenal ulcer and gastric cancer. Gastric and duodenal ulceration had strong statistically significant associations with *H. pylori*, however gastric cancer did not achieve the requisite significance level ( $p = 0.220$ ). There was a lower prevalence of *H. pylori* infection and NSAID-use among patients with non-ulcer dyspepsia in comparison with patients with gastric ulcer, duodenal ulcer and gastric cancer, table 3 and 4.

**Table 3: the prevalence of *H. pylori* infection in non-ulcer dyspepsia, peptic ulcer disease and gastric cancer**

Diagnosis	<i>H. pylori</i> Positive n (%)	<i>H. pylori</i> Negative n (%)	Total	<i>P</i> -value	Chi square (df =1)	Fisher exact test
Non-ulcer dyspepsia	34 (53.1%)	30 (46.9%)	64	0.0001	21.67	0.0001
Gastric ulcer	72 (82.8%)	15 (17.2%)	87	0.033	4.571	0.044
Duodenal ulcer	73 (88.0%)	10 (12.0%)	83	0.001	11.602	0.001
Gastric cancer	19 (65.5%)	10 (34.5%)	29	0.220	1.504	0.255

**Table 4: the prevalence of NSAID-use in non-ulcer dyspepsia, peptic ulcer disease and gastric cancer**

Diagnosis	NSAID-use n (%)	No NSAID-use n (%)	Total	<i>P</i> -value	Chi square (df = 1)	Fisher exact test
Non-ulcer dyspepsia	12 (18.8%)	52 (81.2%)	64	0.006	7.640	0.005
Gastric ulcer	34 (39.1%)	53(60.9%)	87	0.110	2.559	0.194
Duodenal ulcer	32 (38.6%)	51(61.4%)	83	0.157	2.006	0.118
Gastric cancer	8 (27.6%)	21(72.4%)	29	0.536	0.383	0.674

Non-steroidal anti-inflammatory drugs (NSAIDs) were used in 32.6% (n = 79) of patients sampled. These included local/over-the-counter preparations of diclofenac

(75-100mg), ibuprofen (200-400mg) and aspirin (75mg) therapy. Non-steroidal anti-inflammatory drug-use was associated with an increased prevalence of DU in *H. pylori*-infected patients (Table 5).

**Table 5: *H. pylori* infection, NSAID-use and gastro-duodenal disease**

<i>H. pylori</i> and NSAID-use	DU (n/%) $p = 0.003$	GU (n/%) $p = 0.058$	GCA (n/%) $p = 0.141$
Chi square (df= 4)	14.092	7.468	5.468
CLO (+) and NSAID (+): (n=58)	28 (48.3)	28 (48.3)	3 (5.2)
CLO (+) and NSAID (-): (n=123)	45 (36.6)	44 (35.8)	16 (13.0)
CLO (-) and NSAID (+): (n=21)	4 (19.0)	6 (28.6)	5 (23.8)
CLO (-) and NSAID (-): (n=40)	6 (15.0)	9 (22.5)	5 (12.5)

CLO (+): *H. pylori*-positive infection

CLO (-): *H. pylori*-negative infection

NSAID (+): NSAID-use

NSAID (-): No NSAID-use

Following multi-variate analysis of all patients, *H. pylori*-infected patients were more likely than other patients to have peptic ulcer disease, table 5 (GU OR 2.4 CI 1.2-4.8; DU OR 3.5 1.6-7.5). Three (1.2%) study participants were current smokers while 25 (10.3%) had a past history

of smoking. Sixty-two (25.6%) study participants indicated regular alcohol intake in relation to 37 (15.3%) who had a past history of alcohol consumption. There was no demonstrable statistical significant association between smoking, alcohol consumption, herbal medication-use and gastro-duodenal disease.

**Table 6: Relationship between predictor variables and gastro-duodenal disease following multi-variate analysis**

Predictor (%)	GU n=87		DU n=83		GCA n=29		NUD n=64	
	OR	(CI)	OR	(CI)	(OR)	(CI)	(OR)	(CI)
Age	0.7	0.6- 0.9	1.1	0.9-1.3	0.7	0.5-0.9	1.5	1.2-1.8
Herbal use (50)	0.7	0.4-1.3	0.7	0.4-1.2	2.3	0.9-5.4	0.9	0.5-1.7
Smoking (1.2)	0.9	0.4-2.4	1.2	0.5-3.0	1.1	0.3-3.6	0.6	0.2-1.9
Alcohol (25.6)	0.9	0.6-1.5	1.0	0.7-1.6	0.9	0.5-1.8	1.1	0.6-1.8
NSAID-use (32.6)	1.8	0.9-3.2	1.7	0.9-3.1	0.6	0.3-1.6	0.4	0.2-0.8
<i>H.pylori</i> + (78.1)	2.4	1.2-4.8	3.5	1.6-7.5	0.6	0.3-1.5	0.2	0.1-0.4

## Discussion

In this study, *H. pylori* infection was associated with a statistically significant increase in prevalence of duodenal and gastric ulceration, table 2 and 5. Early studies noted a high incidence of *H. pylori* infection in patients with DU8; subsequent reviews confirmed that *H. pylori* is detectable in 80 - 95 percent of these patients<sup>9</sup>. While the association between *H. pylori* and DU is strong, it is not specific as it is also causally linked with GU<sup>10</sup>.

In this study, majority of gastric ulcers were distal in location. Pre-pyloric and antral gastric ulcers accounted for 90.8% of all GUs. Of note, duodenal ulcers and pre-pyloric gastric ulcers share similar patterns of gastric inflammation: an initial antral-predominant gastritis producing an increased acid response with *H. pylori* infection; deemed a marker for duodenal ulcer diathesis<sup>11</sup>.

Gastric cancer did not achieve statistical significance with *H. pylori* in this study. However, epidemiological studies demonstrate a strong correlation between *H. pylori* infection and non-cardia gastric cancer<sup>12</sup>. Additionally, intestinal-type gastric cancer, the dominant gastric adenocarcinoma sampled, has been shown to be more strongly associated with *H. pylori* in comparison with diffuse-type GCA<sup>13,14</sup>. On the contrary, a previous study in Accra, did not find an association between *H. pylori* and gastric cancer<sup>4</sup>. However, the number of GCA cases in our sample population and this preceding study were relatively small, possibly under-estimating the *H. pylori* prevalence.

Non-ulcer dyspepsia had a significantly lower prevalence of *H. pylori* infection (53.1%) when compared with ulcer dyspepsia (83-88%). This would be supported by studies showing no correlation with infection in such patients<sup>4,15-17</sup>. Eradication of *H. pylori* was however associated with a small but significant benefit, with treatment of 14 patients needed to cure one case of NUD<sup>18</sup>.

In Accra, (32.6%) n=79, of patients sampled at the Tertiary Centre, KBTH had a history of NSAID-use, mainly as an analgesic for musculoskeletal pain. Non-steroidal anti-inflammatory drugs are popular because of their versatility and effectiveness as analgesics, anti-pyretics, and as anti-inflammatory agents. In a North-American study, 27% of elderly people were prescribed NSAIDs over a six-month period<sup>19</sup>. The frequency of its use was reportedly higher in another study, where 40% of elderly people

received at least one NSAID prescription annually<sup>19</sup>. It exerts its ulcerogenic effect primarily as a consequence of inhibition of COX-1 thereby reducing mucosal generation of protective prostaglandins such as PGE<sup>2,20</sup>.

In Ghana, we found an increased prevalence of peptic ulcer disease in patients using prescription or over-the-counter NSAIDs, table 4.

NSAID-induced gastric ulcers typically occur in the gastric antrum and pre-pyloric-area and are frequently multiple<sup>21</sup>. A five-year retrospective analysis of NSAID-induced peptic ulceration showed a high incidence of pre-pyloric ulcers in NSAID-users when compared with a control group<sup>21</sup>. Furthermore, peptic ulcers in two or more anatomical sites were more prevalent in the patients on NSAID-therapy<sup>21</sup>. The distribution of DUs and pre-pyloric GUs experienced in this study may therefore reflect the significant use of NSAIDs in an *H. pylori* endemic area.

We also found a statistically significant association between NSAID-use in Ghana with an increased prevalence of DU in *H. pylori*-positive patients ( $p = 0.003$ ). The relationship between NSAID-use, *H. pylori* and peptic ulcer disease is complex: The role of *H. pylori* in NSAID-naïve patients seems to be different from those on long-term therapy. Patients who had eradication of *H. pylori* before NSAID treatment have been shown to have a marked reduction in short-term ulcer risk<sup>22</sup> while *H. pylori* eradication in patients already on long-term NSAID treatment did not decrease incidence of peptic ulcer disease or its complications<sup>23,24</sup>. *H. pylori* therefore exerts a greater influence on ulcer risk on initiation of NSAID therapy than during long-term use.

The cross-sectional design of the study meant we were unable to assess the temporal relationship between risk factors and outcomes. Additionally, patient selection in the main tertiary centre is likely to be associated with relatively more severe cases which may not be generalizable to the wider population. The main objective of the study was to investigate the relationship between *H. pylori*, NSAIDs and gastroduodenal disease therefore patients with oesophageal disease were excluded. This study could not differentiate between duration of NSAID therapy and risk of gastro-duodenal disease in symptomatic patients.

In this study, NSAID gastro-duodenal injury has been shown to be common in a *H. pylori* endemic area, typically presenting as distal gastric ulcers in symptomatic patients.. It also had an additive effect on DU risk in *H. pylori*-positive patients with a higher DU prevalence in such patients. It strengthens the need for awareness on the adverse GI effects of NSAIDs in an *H. pylori* endemic area. Additionally it highlights the need for *H. pylori* eradication to be considered in infected patients who are at increased risk of peptic ulcers especially on initiating long-term NSAID therapy.

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